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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,530	01/17/2002	Jeffrey A. Ledbetter	30906/41458UTL2	8993

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
12/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/053,530	LEDBETTER ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-44,48,102,104,106 and 142-148* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-44,48, 102, 104, 106 and 142-148* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-22, 45-47, 49-101, 103, 105 and 107-141 are cancelled.

Claims 23-24 have been amended.

2. Claims 23-44, 48, 102, 104, 106 and 142-148 are pending and under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections/Rejections

4. The rejection of claims 103 and 105 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of the claims.

5. The rejection of claims 23-44, 48, 102-106 and 142-148 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using the immunoglobulin fusion proteins that mediate ADCC and CDC with the Fc comprising an IgG1 or IgG3 hinge and IgG1 CH2-CH3 domains, does not reasonably provide enablement for the genus of binding domain polypeptides comprising an IgG hinge and just any CH2 and CH3 domains having the property of mediating ADCC is withdrawn in view of applicants' arguments and the amendments to the claims.

6. The provisional rejection of claims 103 and 105 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-53 of copending Application No.11/088,693 is withdrawn in view of the cancellation of the claims.

7. The provisional rejection of claims 103 and 105 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No.10/207,655 in view of Shan et al (The Journal of immunology, 162:6589-6595, 1999, IDS reference EA filed 7/12/02)

and Liu et al (The Journal of Immunology, 139(10):3521-3526, 1987, IDS filed 6/7/04) is withdrawn in view of the cancellation of the claims.

Priority

The following is reiterated for convenience and clarity of the record. The disclosure of a single specific species in prior application USSN 60/367,358 does not provide adequate written support for the myriad of other species of single chain proteins of the present claims, including those that bind to CD19, CD22, CD30 ligand, CD54, CD106, CD2, CD5, CD10, CD27, CD28, CD40, CTLA-4, 4-1BB, 4-1BB ligand, IFN-gamma, IL-4, Il-12, IL-17, IL-17 receptor, CD59, CD48, CD72, CD70, CD86/B7.2, CD40 ligand, CD43, CD83, DEC-205, VLA-4, HER1, HER2, HER3, HER4, EGFR, VEGF, VEGFR, IGF-I, IGF-II, transferrin receptor, estrogen receptor, progesterone receptor, follicle stimulating hormone receptor, rectinoic acid receptor, MUC-1, NY-ESO-1, NA 17-A, Melan-A/MART-1, tyrosinase, Gp-100, MAGE, BAGE, GAGE, CTA class receptors, the HOM-MEL-40 antigen encoded by the SSX2 gene, CEA and PyLT. Further, the present claims are drawn to an IgG1 hinge peptide where the priority application uses an IgG1 hinge and there is no disclosure in the priority document wherein the hinge peptide is an IgG1 in which the number of cysteine residues is reduced to one *and wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted.* Thus, not even the presently claimed CD20 single chain proteins are adequately disclosed in a manner consistent with the first paragraph of 35 U.S.C 112. Again, prior application USSN 60/367,358 discloses the anti-CD20 2H7 scFv fused to human IgG1 hinge-CH2-CH3 as well as 2H7 scFv fused with CD154, which does not provide adequate written support the broader claims of the present application as discussed supra. Therefore, the effective filing date of the presently claimed subject matter is deemed to be that of the instant application, i.e., 1/17/2002. If applicant desires priority prior to

1/17/2002; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

This application repeats a substantial portion of prior Application No. 60/367,358 filed 1/17/2001, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Rejections Maintained

8. The rejection of claims 23-44, 48, 102, 104, 106 and 142-148 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter is maintained. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The repsonse filed 7/19/2007 states that support for the amendment to claims 23-24 can be found at page 23, lines 11-16, and page 24, lines 26-28 of the substitute specification filed 10/22/2003. This has been fully considered but is not found persuasive. It is noted that the substitute specification filed 10/22/2003, contains the identical discsloure as the originally filed specification on 1/17/2002, however, the applicant should point to the discsloure as originally filed for compliance with the description requirement. With respect to the support at pp. 23-24 of the specifictaion as pointed to by applicant, the specification discloses human IgG hinge regions, preferably human IgG1 hinge regions. The claims are drawn to an IgG1 hinge peptide, not a human IgG1 hinge peptide.

Further, even if drawn to a human IgG1 hinge peptide, the disclsoure as pointed to by applicant does not provide adequate written support for the proviso wherein the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. Applicant argues that the specification teaches methods of making polyeptides of the invention having IgG1 hinge regions based on naturally occurring IgG1 hinge regions and teaches that the number of cysteines in the hinge region may be reduced by either deletion or substitution or naturally-occurring cysteine residues (pg. 24, lines 15-19 and Example 5). Applicant states that the specification describes both a wild-type IgG1 hinge and an IgG1 hinge in which the number of cysteines has been reduced and discloses the location for the cysteines in the IgG1 hinge and one of ordinary skill in the art would readily undertsand what is meant by the "first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region ina naturally occurring IgG antibody is not deleted or substituted." Applicants' arguemnts have been fully considered but are not found persuasive. Again, the general disclsoure reducing the number of cysteines in the hinge region would not have led the skilled artisan to the currently claimed limitations, i.e., wherein the first cysteine of the hinge that is resoponsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. The pages and figures as pointed to by applicant generically disclose mutated hinge regions containing one or two cysteine residues and the disclsoure of a scFv-IgG1, in which the hinge cysteines were mutatetd to serine residues (i.e., all of C220→S, C226→S and C229→S) by site-directed mutagenesis and the construct in which the human IgG1 hinge region was substituted with a portion of the human IgA hinge (e.g., see Example. 5, and Fig. 11) does not provide adequate written support for the currently claimed limitations, i.e., wherein the first cysteine of the IgG hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted because there is insufficient guidance

and direction to the subgenus of single chain proteins comprising such. Further, at pg. 29, lines 16-19 of the as filed specifiation it states "The Cys residue of the hinge which makes a disulfide bond with a corresponding Cys of the light chain, to hold the heavy and light chains of the native antibody molecule, can be deleted or, preferably is substituted with, e.g., a Pro residue or the like." (specification at pg. 29). The as filed specification, drawings and claims do not disclose a single species of a single chain polypeptide comprising a binding domain polypeptide comprisng an IgG1 hinge peptide in which the number of cysteine residues is two and the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted and the disclosed preference for its substitution does not provide adequate writtten support for the currently claimed limitations. *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (CCPA 1967) makes clear, one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say "here is my invention". In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure. See id. at 994-95, 154 USPQ at 122; *Fujikawa*, 93 F.3d at 1570-71, 39 USPQ2d at 1905; *Martin v. Mayer*, 823 F.2d 500, 505, 3 USPQ2d 1333, 1337(Fed. Cir. 1987) (It is not a question of whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure. ... Rather, it is a question whether the application necessarily discloses that particular device.) (quoting *Jepson v. Coleman*, 314 F.2d 533, 536, 136 USPQ 647, 649-50(CCPA 1963)). In the instant case, the disclosure pointed to by applicant, generally discloses IgG hinge peptides and discloses that the number of hinge region cysteines can be reduced does not reasonable lead or direct the skilled artisan to the single chain proteins of the instant claims, in which the the first cysteine of the IgG hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. Further, the disclosure wherein "The Cys residue of the hinge which makes a disulfide bond

with a corresponding Cys of the light chain, to hold the heavy and light chains of the native antibody molecule, can be deleted or, preferably is substituted with, e.g., a Pro residue or the like." (specification at pg. 29) would not reasonably lead or direct the skilled artisan to the single chain proteins of the instant claims, in which the the first cysteine of the IgG hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally occurring IgG antibody is not deleted or substituted. It is noted that entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed Cir. 1977).

The claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the presently amended claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ

619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. The provisional rejection of claims 23-44, 48, 102, 104, 106 and 142-148 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-53 of copending Application No.11/088,693 is maintained.

The response filed 7/19/2007 states that applicant will consider filing an necessary terminal disclaimer(s) upon an indication that claimed subject matter is otherwise allowable. The examiner acknowledges applicants remarks, however, the claims are not currently in condition for allowance, no terminal disclaimer has been filed and the rejection is maintained.

11. Claims 24-44, 48, 102, 104, 106 and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No.10/207,655 in view of Shan et al (The Journal of immunology, 162:6589-6595, 1999, IDS reference EA filed 7/12/02) and Liu et al (The Journal of Immunology, 139(10):3521-3526, 1987, IDS filed 6/7/04) is maintained.

The response filed 7/19/2007 states that applicant will consider filing an necessary terminal disclaimer(s) upon an indication that claimed subject matter is otherwise allowable. The examiner acknowledges applicants remarks, however, the claims are not currently in condition for allowance, no terminal disclaimer has been filed and the rejection is maintained.

Applicant is reminded that the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an

application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No.10/207,655, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643